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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/592,928	06/21/2007	Robert Charles Rees	42133-200847	2826

23643 7590 06/26/2008

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EXAMINER	
HARRIS, ALANA M	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
06/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/592,928	REES ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-34,38,39,41,42 and 47-56* is/are pending in the application.

4a) Of the above claim(s) *25-34, 39, 41, 42 and 47-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38 and 54-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group XIII (claims 38 and 54-56) in the reply filed on May 19, 2008 is acknowledged. The traversal is on the ground(s) that the Groups are linked by a novel special technical feature and as amended are linked to form a single general inventive concept, see Remarks, page 9. This is not found persuasive because as set forth in the Election/Restrictions requirement mailed November 21, 2007 Applicants" SEQ ID NO: 1 is not novel, nor is its implementation in a method of treating, see the Requirement, page 4, paragraph 2.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 25-34, 38, 39, 41, 42 and 47-56 are pending.

Claims 35-37, 40, 43-46 have been cancelled.

Claims 38, 41 and 47 have been amended.

Claims 52-56 have been added.

Claims 38 and 54-56 are examined on the merits.

Claim Objections

3. Claims 38 and 54 are objected to because of the following informalities: they reference non-elected subject matter, SEQ ID NO: 2. Correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 38 and 54-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO: 1 and not variants, analogs or derivatives of SEQ ID NO: 1, which are to be implemented in Applicants' methods.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Applicants are not required to disclose every species encompassed by a genus. For example as indicated in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence,

falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Applicants broadly claim methods of preventing and treating cancer comprising administering SEQ ID NO: 1, derivative sequence of SEQ ID NO: 1, and fragment sequences of SEQ ID NO: 1 and derivative sequences. However, Applicant is not entitled, nor is the specification enabled for the use of all variants, analogs and derivatives of SEQ ID NO: 1. Applicant is not permitted to claim all polynucleotides that are encompassed by the claims, hence not entitled to the wide breadth of the claims at issue. There is no description of what sites within the peptide sequence of SEQ ID NO: 1 at which variability may be tolerated and no information regarding the relation of the encoded protein's structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure.

This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

6. Claims 38 and 54-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating cancer comprising administering HLA class-I restricted peptide, SEQ ID NO: 1, does not reasonably provide enablement for prevention of any cancer in a patient, which may or may not

have a tumor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

There is no guidance in the specification as to how to determine and select a population of individuals, which may or may not eventually have cancer. Preventing a disease is just as complex a process. It is not clear what parameters one skilled in the art would use in order to identify a population of subjects in which cancer could be prevented. It is also not clear what symptoms one of skill in the art would need to identify before possibly treating a patient. While it is art known that clinicians are capable of implementing both screening, surveillance and the type of screening test used and the intervals at which it is performed are based on risk stratification, which also serves as the basis for selecting potential candidates for possible prevention. However, like most screening procedures determining whether a population will eventually be struck with a disease is not fool proof.

Additionally, for methods that relate to the prevention of cancer, there is no guidance in the specification for determining the appropriate time prior to the development of tumors to begin the therapy or for identifying patients at risk for developing those tumors. Chamberlain (Expert Opinion on Pharmacotherapy, 1(4): 603-614, 2000) teaches that while vaccines are classically administered prophylactically to evoke an immune response capable of providing protection against infection by the same or similar pathogens for the treatment of infectious diseases, this has not been the approach in the field of cancer immunotherapy. Cancer is not an infectious process.

Cancer cells express a limitless number of antigens and a priori knowledge of whom in the population is at risk for which cancer is lacking (see page 604, 1st column, first full paragraph). The specification provides insufficient guidance in regard to the issues raised above and provides insufficient working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed methods in regard to all cancers with a reasonable expectation of success. In view of the above, one of skill in the art would be forced into undue experimentation to use the claimed compositions as preventative vaccines.

There is insufficient evidence provided enabling one of ordinary skill in the art to determine susceptible cancer candidates within a population. The specification provides neither guidance on nor exemplification of identifying a population of people who may eventually have a tumor. Furthermore, if such a group was identified there is insufficient evidence provided that the tumor growth would be inhibited with the administration of SEQ ID NO: 1.

Moreover, the state of the art reveals cancer vaccines continue to be limited in their effectiveness and in the management of cancers even after several decades of clinical and basic research and especially in the area of spontaneous cancers of man, which Applicants' citing of tumor arising in situ reads upon, see Bodey et al. (Anticancer Research 20: 2665-2676, 2000) page 2668, 1st full paragraph of the 2nd column and column 1, 2nd paragraph. Bodey does support the utility of vaccinations in the treatment of melanomas, however the changing milieu of the cancer the "[u]se of cancer vaccines

to stimulate the immune system may be in vain", see the entire document, particularly bridging paragraph of pages 2737 and 2674.

The criticality of a working example encompassing all of the method steps, especially the treatment of pre-existing neoplasia, is underscored by Gura et al (Science 278: 1041-1042, November 7, 1997) in a discussion of potential shortcomings of extrapolating from animal studies to similar procedures in human cancer patients. Gura teaches that "xenograft tumors don't behave like naturally occurring tumors in humans" (page 1041, second col, second full paragraph) and that there were "gross difference in sensitivity in real tumors in mice and in the clonogenic assay" (page 1042, second col, second full paragraph). Further, Gura teaches that clonogenic assays "cannot tell researchers how anticancer drugs will act in the body" (page 1042, first-second col, bridging paragraph). One skilled in the art would reasonably conclude that evidence obtained in mouse xenograft models would not correlate with results expected in human patients.

Therefore, the complexity and unpredictability of the art to which the invention retains, i.e., in vivo human therapy, suggests the need for some guidance of how to effectively use the claimed methodology to achieve human therapeutic efficacy. There would also need to be some valid amount of direction or guidance, as well as presence or absence of working examples presented in the specification that would enable one skilled in the art to perform the method as presented in the recited claims. It appears that undue experimentation would be required of one skilled in the art to practice the instant claimed invention using the teachings of the specification. See Ex parte

Forman, 230 USPQ 546 BPAI, 1986.]

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 38 and 54-56 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 94/020127 (published 15 September 1994). The WO document discloses Applicants' SEQ ID NO: 1, see below. In anticipation of the instant rejection Applicant's aver the peptide is amongst 200 additional peptide sequences in Table 25, see Remarks filed May 19, 2008, page 9, 1st paragraph. Applicants further arguments noting the disclosed sequence is "...lumped together with fragments from a myriad other unrelated peptides derived from, for example, cytomegalovirus...". These arguments have been carefully considered, but found unpersuasive.

Foremost, Applicants' assertion of this fragment is amongst a number other peptides does not preclude the instant rejection. There is still a very clear teaching of the peptide and its implementation in a method of treating. The disclosed immunogenic peptide is a 9mer that is "...useful in pharmaceutical compositions for both in vivo and

ex vivo therapeutic...applications", see page 3, lines 4-26. The peptide may be administered to relieve and treat several diseases, such as prostate cancer, Grave's disease and scleroderma and has binding affinity for human Class I MHC allele subtypes, in particular HLA-A2.1 alleles, see abstract; page 6, lines 1-34; page 21, line 35-page 28, line 18.

```
RESULT 1
AAR73865
ID   AAR73865 standard; peptide; 9 AA.
XX
AC   AAR73865;
XX
DT   25-MAR-2003  (revised)
DT   22-JUN-1995  (first entry)
XX
DE   Antigen fragment 181, from PAP has binding affinity for HLA-2.1.
XX
KW   antigen; epitope; immunogenic target protein; PSA; HBVc; HBVs; EBV; HIV1;
KW   plasma specific antigen; hepatitis B virus; Epstein Barr;
KW   human immunodeficiency virus; human papilloma virus; p53; c-ERB2; MAGE-1;
KW   melanoma antigen-1; core antigen; surface antigen;
KW   pharmaceutical composition; in vivo; ex vivo; therapeutic; diagnostic;
KW   MHC class I molecule; major histocompatability complex; HLA-A2.1; 9mer;
KW   10mer; anchor; human leukocyte antigen; PLP; 8mer; algorithm prediction;
KW   MBP; CMV; cytomegalovirus; HSV; herpes simplex virus; influenza A; M1;
KW   LCMV; PAP.
XX
OS   Synthetic.
XX
PN   WO9420127-A1.
XX
PD   15-SEP-1994.
XX
PF   04-MAR-1994;   94WO-US002353.
XX
PR   05-MAR-1993;   93US-00027146.
PR   04-JUN-1993;   93US-00073205.
PR   29-NOV-1993;   93US-00159184.
XX
PA   (CYTE-) CYTEL CORP.
XX
PI   Grey HM,  Sette A,  Sidney J,  Kast W;
XX
DR   WPI; 1994-302678/37.
XX
PT   Immunogenic peptide(s) having an HLA-A2.1 binding motif - used for
PT   treatment or prophylaxis of cancer, virus infection or autoimmune
PT   diseases.
XX
PS   Disclosure; Page 87; 138pp; English.
XX
CC   AAR73685-876 are potential peptide binders of HLA-A2.1 motif. Using
CC   motifs disclosed in the invention, these peptides were screened for
CC   further motifs. Only peptides with binding affinity of at least 1%
CC   (binding affinity is expressed as an IC50 value) as compared to the
CC   standard peptide (AAR71293) in assays. This peptide from PAP (sic) has a
CC   binding value of 1.3000. The peptides of the invention can induce
CC   cytotoxic T lymphocytes which can react with target cells. They can be
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CC   used for the treatment or prophlyaxis of cancer, eg. prostate cancer or
CC   lymphoma, etc. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ   Sequence 9 AA;

  Query Match             100.0%;  Score 50;  DB 2;  Length 9;
  Best Local Similarity   100.0%;  Pred. No. 2.3e+06;
  Matches    9;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 ILLWQPIPV 9
              |||||||||
Db          1 ILLWQPIPV 9
```

9. Claims 38 and 54-56 rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 7,084,249 B1 (filed July 29, 1999). The patent discloses the sequence 32, the same peptide as Applicants' SEQ ID NO: 1, see sequence alignment. This peptide is a tumor associated antigen derived from prostate acid phosphate (PAP) and included in an anti-tumor vaccine to prevent or treat prostate cancer, see column 1, lines 11-24; column. 3, lines 45-55; and Table 6, column 27. The PAP peptides are immunogenic CTL epitopes in HLA-A2 transgenic H-2 D^b, β2m double knockout mice, see Example 2 beginning in column 25.

```
RESULT 1
US-09-744-804A-32
; Sequence 32, Application US/09744804A
; Patent No. 7084249
; GENERAL INFORMATION:
;  APPLICANT: Yeda Research & Development Company Limited at the
;  APPLICANT:  Bio-Technology General Corp.
;  TITLE OF INVENTION: Tumor Associated Antigen Peptides and Use of Same as
;  TITLE OF INVENTION:  Anti-Tumor Vaccines
;  FILE REFERENCE: EISENBACH=3
;  CURRENT APPLICATION NUMBER: US/09/744,804A
;  CURRENT FILING DATE:  2001-06-20
;  PRIOR APPLICATION NUMBER: IL 125608
;  PRIOR FILING DATE: 1998-07-30
;  NUMBER OF SEQ ID NOS: 78
;  SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 32
;   LENGTH: 9
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-09-744-804A-32

  Query Match             100.0%;  Score 50;  DB 3;  Length 9;
  Best Local Similarity   100.0%;  Pred. No. 8e+05;
  Matches    9;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 ILLWQPIPV 9
```

```
                 |||||||||
Db          1 ILLWQPIPV 9
```

10. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571)272-0831. The Examiner works a flexible schedule, however she can normally be reached between the hours of 7:30 am to 6:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Alana M. Harris, Ph.D.
23 June 2008
/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643